REMARKS

Claims 7-10, 12, 14, and 23 are now pending in the present application, claims 24-27 having been cancelled by the above amendments. Claim 7 has been amended to recite that the acetoacetyl-CoA reductase contains the amino acid sequence of a naturally occurring reductase, a limitation supported, for example, at pages 5-6, bridging sentence, of the specification. In addition, claim 7 now incorporates the limitation of claim 24, now cancelled. The significant differences between the four different types of reductase enzymes are described at pages 3-4, bridging paragraph, of the specification. Dependent claim 10 has been narrowed by deleting genera of reductases that encompass non-naturally occurring amino acid sequences. No new matter has been added by the above amendments.

In the last response entered into the application, applicant added new claims, including claims 25-27. The Examiner has now withdrawn from consideration claims 25-27 as been drawn to an independent or distinct invention. To facilitate prosecution, applicants have cancelled claims 25-27.

Claims 7-10, 12, 14, and 23 are rejected under 35 U.S.C. § 112, first paragraph, for a failure of the specification to provide adequate enablement or written description support for the full scope of the claims. Applicant has now limited claim 7, the only pending independent claim, to acetoacetyl-CoA reductases that contain the amino acid sequence of a naturally occurring enzyme. Since, in the last response entered, applicant has pointed out that naturally occurring reductases and genes encoding them are known to one skilled in the art who has read the specification, it is submitted that the claims are now commensurate with the support provided. Accordingly, the rejection should be withdrawn.

Claim 10 is rejected under 35 U.S.C. § 112, second paragraph, for recitation of the allegedly indefinite term "stringent conditions." Applicant has deleted the portion of claim 10 that includes this term, rendering the rejection moot.

Claims 7-10, 14, 23, and 24 are rejected under 35 U.S.C. § 103(a) as obvious over Matsuyama et al. (U.S. Patent No. 5,559,030) in view of Peoples et al. (U.S. Patent No. 5,229,279) or Summerville et al. (WO 93/02187). Peoples and Summerville are cited by the Examiner to show that cloned acetoacetyl-CoA reductases are known and have been used in the

reaction for which the enzyme is named, as exemplified in Peoples' Fig. 1. In that sense, Peoples and Summerville are cumulative references.

Applicant thanks the Examiner and his Supervisor for the constructive telephonic interview conducted with the undersigned on January 30, 2001. In that interview, the Examiner and Supervisor supported the single outstanding obviousness rejection by, in part, pointing out the similarities of the chemical structure of Matsuyama's substrate (col. 2, line 10) and People's substrate for acetoacetyl-CoA reductase (Fig. 1). Applicant indicated that there were significant structural differences between the two, and the motivation to, e.g., include a halogen on Peoples' substrate was completely lacking. Applicant also pointed out that, although acetoacetyl-CoA reductase has been isolated at least since 1977 (see col. 1, lines 65-67, of Peoples) and the benefits of producing (S)-4-halo-3-hydroxybutyric acid ester have been known at least since the early 1980's (see page 1, first paragraph of BACKGROUND OF THE INVENTION of the specification), no one other than applicant has realized that a known enzyme (acetoacetyl-CoA reductase) can be used to facilitate a known commercially valuable chemical reaction. This is surely strong indicia of nonobviousness and shows that some structural similarity between Matsuyama's substrate and Peoples' substrate is insufficient to motivate the skilled artisan to use acetoacetyl-CoA reductase in the reaction recited in claim 7. Consequently, the Examiner's and Supervisor's contention that motivation to combine the references can arise merely from substrate similarities in Matsuyama and Peoples appears to be hindsight reconstruction. Applicant respectfully asks the Examiner to cast his mind back to the time the present invention was made and ask whether it would have been obvious to achieve the invention, particularly in light of the above discussion.

Applicant submits that all of the claims are now in condition for allowance, which action is requested. Filed herewith is a Petition for Automatic Extension with the required fee, taking into account the Petition for Automatic Extension already filed on February 28, 2001. Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

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Version With Markings To Show Changes Made

In the Claims:

7. (Amended) A method for producing (S)-4-halo-3-hydroxybutyric acid ester, the method comprising asymmetrically reducing a 4-halo-acetoacetic acid ester or its derivative with a purified acetoacetyl-CoA reductase that can participate in a poly-β-hydroxy fatty acid biosynthesis system, the purified acetoacetyl-CoA reductase comprising the amino acid sequence of a naturally occurring acetoacetyl-CoA reductase.

10. (Amended) The method of claim 7, wherein said acetoacetyl-CoA reductase [is selected from the group consisting of:

(a) a protein comprising] comprises the amino acid sequence of SEQ ID NO: 9[;

(b) a protein (1) comprising a modified amino acid sequence of SEQ ID NO: 9 in which one or more amino acid residues are added, deleted, or substituted and (2) capable of asymmetrically reducing 4-haloacetoacetic acid ester or its derivatives to produce (S)-4-halo-3-hydroxybutyric acid ester; and

(c) a protein (1) encoded by DNA that hybridizes under stringent conditions to DNA consisting of SEQ ID NO: 10 and (2) capable of asymmetrically reducing 4-haloacetoacetic acid ester or its derivatives to produce (S)-4-halo-3-hydroxybutyric acid ester].